

1 The claims:

2
3 1. A dosage form comprising a drug layer comprising 8 mg of
4 hydromorphone, 67.8 mg of poly(ethylene oxide) of 200,000 molecular
5 weight, 4 mg of poly(vinyl pyrrolidone), and 0.2 mg of a lubricant; a delivery
6 layer comprising 37.8 mg of poly(ethylene oxide) possessing a 2,000,000
7 molecular weight, 18 mg of sodium chloride, 3 mg of hydroxypropylmethyl-
8 cellulose of 9,200 molecular weight, 0.6 mg of a colorant, and 0.15 mg of a
9 lubricant; a semipermeable wall comprising 27.2 mg of cellulose acetate of
10 39.8% acetyl content, and 0.275 mg of polyethylene glycol of 3,350
11 molecular weight; a passageway in the wall; and a controlled rate of release
12 of 0.427 mg/hr for 17.3 hours.

13
14 2. A dosage form comprising 32 mg of hydromorphone, 119.6 mg
15 of poly(ethylene oxide) possessing a 200,000 molecular weight, 8 mg of
16 poly(vinyl pyrrolidone) of 42,000 molecular weight, and 0.4 mg of magnesium
17 stearate; a delivery layer comprising 76.49 mg of poly(ethylene oxide) of
18 2,000,000 molecular weight, 36 mg of sodium chloride, 6 mg of
19 hydroxypropylmethylcellulose of 9,200 molecular weight, 0.3 mg of
20 magnesium stearate, 1.2 mg of a colorant, and 0.012 mg of an antioxidant; a
21 semipermeable wall comprising 29.6 mg of cellulose acetate comprising an
22 acetyl content of 39.8%, and 0.29 mg of polyethylene glycol possessing a
23 3,350 molecular weight, which wall surrounds the layers; a passageway in
24 the dosage form; and a controlled rate of release of 1.811 mg/hr for 16.1
25 hours.

26
27 3. A dosage form comprising 64 mg of hydromorphone, 138.6 mg
28 of poly(ethylene oxide) possessing a 200,000 molecular weight, 10.7 mg of
29 poly(vinyl pyrrolidone) of 42,000 molecular weight, and 0.53 mg of a
30 lubricant; a delivery layer comprising 104.53 mg of poly(ethylene oxide) of

1 2,000,000 molecular weight, 49.2 mg of an osmagent, 8.2 mg of
2 hydroxypropylmethylcellulose of 9,200 molecular weight, 1.64 mg of a
3 colorant, 0.41 mg of a lubricant, and 0.123 mg of an antioxidant; a
4 semipermeable wall comprising 38.61 mg of cellulose acetate comprising a
5 39.8% acetyl content, and 0.39 mg of polyethylene glycol of 3,350 molecular
6 weight, which wall surrounds the layers; a passageway in the wall; and a
7 controlled rate of release of 3.77 mg/hr of hydromorphone over 15.3 hours.
8

9 4. A dosage form comprising 16 mg of hydromorphone, 135.6 mg
10 of poly(ethylene oxide) of 200,000 molecular weight, 8 mg of poly(vinyl
11 pyrrolidone) of 42,000 molecular weight, and 0.4 mg of a lubricant; a delivery
12 layer comprising 76.49 mg of poly(ethylene oxide) of 2,000,000 molecular
13 weight, 36 mg of an osmagent, 6 mg of hydroxypropylmethylcellulose of
14 9,200 molecular weight, 1.2 mg of a colorant, 0.3 mg of a lubricant, and 0.12
15 mg of an antioxidant; a semipermeable wall that surrounds the layers
16 comprising 27.52 mg of cellulose acetate of 39.8% acetyl content, and 0.27
17 mg of polyethylene glycol of 3,350 molecular weight; a passageway in the
18 dosage form; and a controlled rate of release of 0.957 mg/hr for 15.0 hours.
19

20 5. A dosage form comprising: a drug layer comprising 8 mg of a
21 member selected from the group consisting of hydromorphone and
22 hydromorphone pharmaceutically acceptable salt, 84.70 wt% poly(ethylene
23 oxide), 5 wt% poly (vinylpyrrolidone), 0.05 wt% butylated hydroxytoluene and
24 0.25 wt% magnesium stearate; an expandable layer comprising 63.675 wt%
25 poly(ethylene oxide), 30 wt% of sodium chloride, 5 wt% of
26 hydroxypropylmethylcellulose, 0.075 wt% of butylated hydroxytoluene, 1 wt%
27 of a colorant, and 0.25 wt% of magnesium stearate; a semipermeable wall
28 comprising 99 wt% cellulose acetate and 1 wt% polyethylene glycol that
29 surrounds the drug and expansion layers; and, an exit in the wall for
30 delivering hydromorphone from the dosage form.

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1 6. The dosage form according to claim 5, wherein the drug layer
2 comprises 16 mg of a member selected from the group consisting of
3 hydromorphone and a pharmaceutically acceptable salt.

4
5 7. The dosage form according to claim 5, wherein the drug layer
6 weighs 80 mgs.

7
8 8. The dosage form according to claim 6, wherein the drug layer
9 weighs 160 mg.

10
11 9. The dosage form according to claim 5, wherein the expandable
12 layer weighs 60 mg.

13
14 10. The dosage form according to claim 6, wherein the expandable
15 layer weighs 120 mg.

16
17 11. The dosage form according to claim 5, wherein the dose of
18 hydromorphone comprises 10 wt% of the drug layer.

19
20 12. The dosage form according to claim 6, wherein the dose of
21 hydromorphone comprises 10 wt% of the drug layer.

22
23 13. The dosage form according to claim 5, wherein the expandable
24 layer weighs 60 mg.

25
26 14. The dosage form according to claim 5, wherein the expandable
27 layer weighs 120 mg.

28
29 15. A dosage form comprising: a drug layer comprising 32 mg of a
30 member selected from the group consisting of hydromorphone and

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1 hydromorphone pharmaceutically acceptable salt, 74.75 wt% poly(ethylene
2 oxide), 5 wt% poly(vinylpyrrolidone) and 0.25 wt% magnesium stearate, an
3 expandable layer comprising 63.675 wt% poly(ethylene oxide), 30 wt%
4 sodium chloride, 5 wt% hydroxypropylmethylcellulose, 0.075 butylated
5 hydroxytoluene, 1 wt% colorant, and 0.25 wt% magnesium stearate; a
6 semipermeable wall comprising 99 wt% cellulose acetate and 1 wt%
7 poly(ethylene glycol), which wall surrounds the drug and expandable layers;
8 and, an exit in the wall for delivering hydromorphone from the dosage form.

9
10 16. The dosage form according to claim 14, wherein the drug layers
11 weighs 160 mg.

12
13 17. The dosage form according to claim 14, wherein the expandable
14 layer weighs 120 mg.

15
16 18. The dosage form according to claim 14, wherein the dose of
17 hydromorphone is 20 wt% of the drug layer.

18
19 19. A dosage form for delivering orally hydromorphone to a patient
20 in need of relief from pain, wherein the dosage form comprises: a drug layer
21 comprising 64 mg of a member selected from the group consisting of
22 hydromorphone and its pharmaceutically acceptable salt, 64.75 mg of a
23 poly(alkylene oxide), 5 wt% of a poly(vinylpyrrolidone) and 0.25 wt% of a
24 lubricant; an expandable layer comprising 63.675 wt% of a poly(alkylene
25 oxide), 30 wt% of an osmotically effective solute, 5 wt% of a hydroxypropyl-
26 alkylcellulose, 0.075 wt% of an antioxidant, 1 wt% of a colorant, and 0.25 wt%
27 of a lubricant; a semipermeable wall that surrounds the layers comprising 99
28 wt% cellulose acetate, and 1 wt% poly(ethylene glycol); and, an exit in the
29 semipermeable wall for delivering the hydromorphone to the patient to
30 provide relief from pain.

1 20. The dosage form according to claim 15, wherein the drug layer
2 weighs 214 mg.

3
4 21. The dosage form according to claim 15, wherein the expandable
5 layer weighs 164 mg.

6
7 22. The dosage form according to claim 15, wherein the dose of
8 hydromorphone is 30 wt% of the drug layer.

9
10 23. A dosage form comprising a drug layer that weighs 80 mg and
11 comprises 10.5% hydromorphone hydrochloride, 84.23% poly(ethylene oxide)
12 having a 200,000 molecular weight, 5% poly(vinylpyrrolidone), 0.02%
13 butylated hydroxytoluene, and 0.25% magnesium stearate; an expandable
14 layer that weighs 60 mg and comprises 64.3% poly(ethylene oxide)
15 possessing a 2,000,000 molecular weight, 30.00% sodium chloride, 5%
16 hydroxypropylmethylcellulose, black iron oxide and lactose, 0.25%
17 magnesium stearate, and 0.05 butylated hydroxytoluene; a membrane that
18 surrounds the drug and expandable layers comprising 99% cellulose acetate
19 and 1% polyethylene glycol; and an exit in the membrane for delivering the
20 hydromorphone from the dosage form.

21
22 24. The dosage form according to claim 23, wherein the dosage
23 form comprises 0.4% or 1% of black iron oxide and lactose.

24
25 25. The dosage form according to claim 23 on, wherein the
26 poly(vinylpyrrolidone) comprises a molecular weight of 38,000 to 42,000, the
27 hydroxypropylmethylcellulose comprises a molecular weight of 9,200 to
28 11,300, and the expandable layer weighs 54 to 66 mg.

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1 26. The dosage form according to claim 23 wherein the cellulose
2 acetate comprises a 39.8% acetyl content and the polyethylene glycol
3 comprises a 3,350 to 4,000 molecular weight.

4
5 27. The dosage form according to claim 23, wherein the membrane
6 is a wall and weighs 25 mg.

7
8 28. A dosage form comprising a drug layer that weighs 152.4 mg
9 and comprises 10.5% hydromorphone hydrochloride, 84.23% poly(ethylene
10 oxide) of 200,000 molecular weight, 5% poly(vinylpyrrolidone), 0.02%
11 butylated hydroxytoluene, and 0.25% magnesium stearate; an expandable
12 layer comprising 64.3% poly (ethylene oxide) possessing a 2,000,000
13 molecular weight, 30.00% sodium chloride, 5% hydroxypropylmethylcellulose,
14 black iron oxide and lactose, 0.25% magnesium stearate, and 0.05%
15 butylated hydroxytoluene; a membrane that surrounds the layer and
16 comprises 99% cellulose acetate and 1% polyethylene glycol; and an exit in
17 the membrane for delivering the drug from the dosage form.

18
19 29. The dosage form according to claim 28, wherein the dosage
20 form comprises 0.4% or 1% of black iron oxide and lactose.

21
22 30. The dosage form according to claim 28, wherein the
23 poly(vinylpyrrolidone) comprises a 38,000 to 42,000 molecular weight, the
24 hydroxypropylmethylcellulose comprises a 9,200 to 11,300 molecular weight,
25 and the expandable layer weighs 122 to 134 mg.

26
27 31. The dosage form according to claim 28 wherein, the cellulose
28 acetate comprises a 39.8% acetyl content, and the polyethylene glycol
29 comprises a 3,350 to 4,000 molecular weight.

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1 32. The dosage form according to claim 28, wherein the membrane
2 is a semipermeable wall and weighs 27 mg.

3
4 33. The dosage form according to claim 28, wherein the black iron
5 oxide and the lactose are present as a 95:5 mix.

6
7 34. A dosage form comprising a drug layer that weighs 160 mg and
8 comprises 20% hydromorphone hydrochloride, 74.68% poly(ethylene oxide)
9 possessing a 200,000 molecular weight, 5% poly(vinylpyrrolidone), 0.02%
10 butylated hydroxytoluene, and 0.25% magnesium stearate; an expandable
11 layer comprising 63.672% poly(ethylene oxide) possessing a 2,000,000
12 molecular weight, 30.00% sodium chloride, 5% hydroxypropylmethyl-
13 cellulose, 1% black iron oxide and lactose, 0.25% magnesium stearate, and
14 0.05% butylated hydroxytoluene; a rate controlling membrane that surrounds
15 both layers and comprises 99% cellulose acetate and 1% polyethylene glycol;
16 and an exit in the membrane for delivering the drug from the dosage form.

17
18 35. The dosage form according to claim 34 wherein, the drug layer
19 comprises 0.05% ferric oxide yellow.

20
21 36. The dosage form according to claim 34 wherein, the
22 poly(vinylpyrrolidone) possesses a 38,000 to 42,000 molecular weight, the
23 hydroxypropylmethylcellulose, and the expandable layer weighs 114 to 126
24 mg.

25
26 37. The dosage form according to claim 34 wherein, the cellulose
27 acetate comprises an acetyl content of 39.8% and the polyethylene glycol
28 comprises a 3,350 to 4,000 molecular weight.

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38. The dosage form according to claim 34 wherein, the membrane is a semipermeable wall and weighs 29 mg.

39. The dosage form according to claim 34 wherein, the black iron oxide and lactose comprise a 95:5 mix and is a colorant.

40. A dosage form comprising a drug layer that weighs 213.3 mg and comprises 30% hydromorphone hydrochloride, 64.73% poly(ethylene oxide) possessing a 200,000 molecular weight, 5% poly(vinylpyrrolidone), 0.02% butylated hydroxytoluene and 0.25% magnesium stearate; an expandable layer comprising 64.3% poly(ethylene oxide) possessing a 2,000,000 molecular weight, 30.003% sodium chloride, 5% hydroxypropylmethyl-cellulose, black iron oxide and lactose, 0.25% magnesium stearate, and 0.05% butylated hydroxytoluene; a membrane that surrounds the layers and comprises 99% cellulose acetate and 1% polyethylene glycol; and an exit in the membrane for delivering the hydromorphone from the dosage form.

41. The dosage form according to claim 40, wherein the dosage form comprises 0.4% or 1% black iron oxide and 0.05% butylated hydroxytoluene.

42. The dosage form according to claim 40 wherein, the poly(vinylpyrrolidone) comprises a 38,000 to 42,000 molecular weight, the hydroxypropylmethylcellulose comprises a 9,200 to 11,300 molecular weight, and the expandable layer weighs 156 to 172 mg.

43. The dosage form according to claim 40 wherein, the cellulose acetate comprises an acetyl content of 39.8% and the polyethylene glycol comprises a 3,350 to 4,000 molecular weight.

1 44. The dosage form according to claim 40 wherein, the membrane
2 is a semipermeable wall and weighs 40 mg.

3
4 45. The dosage form according to claim 40 wherein the black iron
5 oxide and the lactose comprise a 95:5 mix, and is a colorant.

6
7 46. An extended-release dosage form comprising 1 mg to 500 mg
8 of a member selected from the group consisting of hydromorphone and
9 hydromorphone pharmaceutically acceptable salt that is administered orally to
10 a patient in an extended-release time up to 24 hrs for the relief of pain.

11
12 47. An extended-release dosage form comprising 1 mg to 500 mg
13 of a member selected from the group consisting of hydromorphone and its
14 pharmaceutically acceptable salt that is administered orally to a patient in a
15 dose of 0.04 mg/hr to 20 mg/hr up to 24 hrs for the relief of pain associated
16 with an infection, surgery, cancer, trauma, colic, disease, infarction, burns,
17 cold, cough, ulcer, hepatic, and renal pain.

18
19 48. An extended-release pharmaceutical formulation comprising 1
20 mg to 500 mg of a total dose of a member selected from the group consisting
21 of hydromorphone and hydromorphone pharmaceutically acceptable salt in a
22 pharmaceutically acceptable carrier in a delivery dose pattern of from 0 to
23 20% in 0 to 4 hrs, 20 to 50% in 0 to 8 hrs, 55 to 85% in 0 to 14 hrs, and 80 to
24 100% in 0 to 24 hrs for achieving a therapeutically effective blood level over
25 the delivery pattern.

26
27 49. An extended-release pharmaceutical formulation comprising 1
28 mg to 500 mg dose of a member selected from the group consisting of
29 hydromorphone and hydromorphone pharmaceutically acceptable salt that is
30 delivered in a therapeutic dose of from 0 to 20% in 0 to 4 hrs, 20 to 50% in 0

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1 to 8 hrs, 55 to 85% in 0 to 14 hrs, and 75 to 100% in 0 to 24 hrs for the relief
2 of pain associated with infection, surgery, cancer, trauma, colic, disease,
3 infarction, burns, cold, cough, ulcer, hepatic, and renal pain.

4
5 50. A method of producing a plasma concentration of
6 hydromorphone in a patient in need of hydromorphone, wherein the method
7 comprises orally admitting into the patient a dosage form comprising 1 mg to
8 500 mg of hydromorphone that is administered as a controlled rate over a
9 continuous time up to 24 hours for hydromorphone to enter the plasma for
10 producing the intended hydromorphone therapy.

11
12 51. A method for producing hydromorphone therapy in a patient,
13 wherein the method comprises administering orally to the patient a dose of
14 hydromorphone that produces a first plasma hydromorphone concentration, a
15 second elevated plasma hydromorphone concentration, and a third
16 continuous plasma hydromorphone concentration for producing
17 hydromorphone therapy in the patient.

18
19 52. A method for providing hydromorphone pain relief to a patient,
20 wherein the method comprises orally administering to the patient an effective
21 dose of hydromorphone that produces a first plasma level in from 0 to 8
22 hours, a second higher plasma, hydromorphone level in 8 to 12 hours, and a
23 third extended plasma hydromorphone level in up to 24 hours to provide
24 hydromorphone pain relief.

25
26 53. A method for providing hydromorphone to a patient, wherein the
27 method comprises admitting orally into the patient a dosage form comprising
28 10 to 100 mg of hydromorphone that is administered at a rate of 0.4 to 3.7
29 mg/hr up to 24 hrs for providing hydromorphone to the patient.

- 1 54. A method for providing a plasma concentration of
- 2 hydromorphone to a patient, wherein the method comprises administering
- 3 orally into the gastrointestinal tract of the patient 2 to 75 mg of
- 4 hydromorphone to produce from greater than zero ng/ml to twenty-five ng/ml
- 5 plasma concentration.

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